

WHAT IS CLAIMED IS:

1. A modified biological molecule comprising a biological molecule modified by reaction with a compound having the formula: $R_1 - X - R_2$, wherein R_1 is a cyclic ether group or an amino group, R_2 is an alkoxysilane group and X is a moiety chemically suitable for linking the cyclic ether group or the amino group to the alkoxysilane group.

2. The modified biological molecule of claim 1, wherein the cyclic ether is a compound comprising an epoxide group.

3. The modified biological molecule of claim 2, wherein the epoxide is ethylene oxide.

4. The modified biological molecule of claim 1, wherein the cyclic ether is an oxirane group.

5. The modified biological molecule of claim 1, wherein the cyclic ether is a compound comprising an aromatic hydrocarbon epoxide group.

6. The modified biological molecule of claim 1, wherein the R_1 group reacts with the biological molecule.

7. The modified biological molecule of claim 6, wherein the R_1 group is covalently bound to the biological molecule.

8. The modified biological molecule of claim 1, wherein the biological molecule comprises a polypeptide, a peptide or a peptidomimetic.

9. The modified biological molecule of claim 1, wherein the biological molecule comprises a polysaccharide, or an analog or a mimetic thereof.

10. The modified biological molecule of claim 1, wherein the biological molecule comprises a lipid, or an analog or a mimetic thereof.

11. The modified biological molecule of claim 1, wherein the biological molecule comprises a small molecule.

12. The modified biological molecule of claim 1, wherein the biological molecule comprises a nucleic acid or an analog or mimetic thereof.

13. The modified biological molecule of claim 12, wherein the nucleic acid comprises a DNA or an RNA.

14. The modified biological molecule of claim 12, wherein the nucleic acid reacts with the R_1 group at its 5' end.

15. The modified biological molecule of claim 12, wherein the nucleic acid is an oligonucleotide.

16. The modified biological molecule of claim 12, wherein the nucleic acid comprises a telomeric structure.

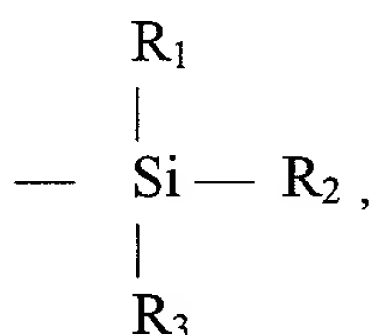
17. The modified biological molecule of claim 12, wherein the nucleic acid comprises a chromatin structure.

18. The modified biological molecule of claim 1, wherein cyclic ether is an epoxide group and the alkoxysilane is $-\text{Si}(\text{OCH}_3)_3$, $-\text{Si}(\text{OC}_2\text{H}_5)_3$, $-\text{Si}(\text{OCH}_3)\text{H}_2$, $-\text{Si}(\text{OCH}_3)(\text{CH}_3)_2$, or $-\text{Si}(\text{OCH}_3)_2\text{CH}_3$.

19. The modified biological molecule of claim 1, wherein cyclic ether is an epoxide group and the compound is 3-glycidoxypropyltrimethoxysilane (GPTS).

20. The modified biological molecule of claim 1, wherein the R₁ amino group comprises a primary amino group.

21. The modified biological molecule of claim 1, wherein R₁ is an amino group and the alkoxy silane is selected from the group consisting of —Si(OCH₃)₃, —Si(OC₂H₅)₃ and



wherein R₁, R₂ and R₃ are selected from the group consisting of —H, —CH₃, —OCH₃, and —OC₂H₅, and provided that at least one of R₁, R₂ or R₃ is either —OCH₃ or —OC₂H₅.

22. The modified biological molecule of claim 1, wherein R₁ is an amino group and the compound is 3-aminopropyltriethoxysilane.

23. An article of manufacture comprising an arrayed plurality of biological molecules covalently bound to a surface,

wherein, before attachment to the surface, the biological molecules are modified by reaction with a compound having the formula: R₁ — X — R₂, wherein R₁ is a cyclic ether group or an amino group, R₂ is an alkoxy silane group and X is a moiety chemically suitable for linking the cyclic ether group or the amino group to the alkoxy silane group, and upon attachment to the surface the modified biological molecules are covalently bound to the surface;

wherein each biological molecule is attached to the surface on at least one discrete and known location to form a cluster of substantially identical biological molecules.

24. The article of manufacture of claim 23, wherein the surface is a glass.

25. The article of manufacture of claim 23, wherein the surface is a mica or a quartz.

26. The article of manufacture of claim 23, wherein the surface is a metal oxide surface.

27. The article of manufacture of claim 26, wherein the metal oxide surface is selected from the group consisting of an alumina (Al_2O_3), a titania (TiO_2), a SnO_2 , a RuO_2 , or a PtO_2 .

28. The article of manufacture of claim 23, wherein the surface is selected from the group consisting of a polystyrene, a polyester, a polycarbonate, a polyethylene, a polypropylene, and a nylon.

29. The article of manufacture of claim 23, wherein the modified biological molecules are covalently bound to the surface via the R_2 group.

30. The article of manufacture of claim 23, wherein the biological molecules are derived from a human.

31. The article of manufacture of claim 23, wherein the biological molecules are derived from a mouse.

32. The article of manufacture of claim 23, wherein the biological molecules comprise a nucleic acid, or an analog or a mimetic thereof.

33. The article of manufacture of claim 32, wherein the nucleic acid comprises a DNA or an RNA.

34. The article of manufacture of claim 32, wherein the nucleic acid is an oligonucleotide.

35. The article of manufacture of claim 23, wherein the biological molecule comprises a polypeptide, a peptide or a peptidomimetic.

5 36. The article of manufacture of claim 23, wherein the biological molecule comprises a polysaccharide, or an analog or a mimetic thereof.

37. The article of manufacture of claim 23, wherein the biological molecule comprises a lipid, or an analog or a mimetic thereof.

10 38. The article of manufacture of claim 23, wherein the biological molecule comprises a small molecule.

15 39. The article of manufacture of claim 32, wherein the nucleic acid reacts with the R₁ group at its 5' end.

40. The article of manufacture of claim 32, wherein the nucleic acid comprises a plurality of fragments of a genomic nucleic acid.

20 41. The article of manufacture of claim 40, wherein the genomic nucleic acid is derived from a normal cell.

42. The article of manufacture of claim 40, wherein the genomic nucleic acid is derived from a cell suspected of having a chromosomal defect or abnormality.

25 43. The article of manufacture of claim 42, wherein the cell suspected of having a chromosomal defect or abnormality is a tumor cell.

30 44. The article of manufacture of claim 40, wherein the fragments of genomic nucleic acid further comprise a cloning vehicle.

45. The article of manufacture of claim 44, wherein the cloning vehicle comprises a bacterial artificial chromosome (BAC).

46. The article of manufacture of claim 44, wherein the cloning vehicle comprises a plasmid, a cosmid, a bacteriophage P1-derived vector (PAC), a yeast artificial chromosome (YAC) or a mammalian artificial chromosome (MAC).

47. The article of manufacture of claim 32, wherein the nucleic acid comprises a plurality of CpG island tags.

48. The article of manufacture of claim 40, wherein the fragments of genomic nucleic acid comprise sequences representing at least one substantially complete chromosome or at least one defined section of a chromosome.

49. The article of manufacture of claim 40, and each genomic nucleic acid fragment has been mapped to a known location on the chromosome.

50. The article of manufacture of claim 40, wherein the genomic nucleic acid fragments have a size no more than about 1.2 megabase.

51. The article of manufacture of claim 50, wherein genomic nucleic acid fragments are no more than about 1.0 megabase in size.

52. The article of manufacture of claim 23, wherein each cluster consists of between about 10 and about 200 substantially identical copies of a biological molecule.

53. The article of manufacture of claim 23, wherein the surface consists of less than about 400 clusters per square centimeter.

54. The article of manufacture of claim 23, wherein each cluster is about 50 microns in diameter or smaller.

55. The article of manufacture of claim 54, wherein each cluster is about 25 microns in diameter or smaller.

5 56. An article of manufacture comprising an array of cloned genomic nucleic acid fragments representing a defined subsection of or a substantially complete chromosome,

10 wherein, before attachment to the surface, the cloned fragments are modified by reaction with a compound having the formula: $R_1 - X - R_2$, wherein R_1 is an epoxide group, R_2 is an alkoxysilane group and X is a moiety chemically suitable for linking the epoxide group and the alkoxysilane group, and the modified cloned fragments are covalently bound to the surface;

15 wherein each array-bound cloned fragment has been mapped to a known location on a chromosome.

20 57. A kit comprising an article of manufacture as set forth in claim 23 and printed matter, wherein the printed matter comprises instructions on hybridizing a sample of nucleic acid to an array-bound nucleic acid.

25 58. A method for identifying a specific binding partner, comprising:
(a) providing an article of manufacture comprising an arrayed plurality of biological molecules covalently bound to a surface, wherein, before attachment to the surface, the biological molecules are modified by reaction with a compound having the formula: $R_1 - X - R_2$, wherein R_1 is an cyclic ether group or an amino group, R_2 is an alkoxysilane group and X is a moiety chemically suitable for linking the cyclic ether group or the amino group to the alkoxysilane group, and upon attachment the modified biological molecules are covalently bound to the surface,

30 wherein each biological molecule is attached to the surface on at least one discrete and known location to form a cluster of identical biological molecules;

(b) providing a sample of biological molecules;

(c) contacting the sample of step (b) with the array-bound biological molecules as set forth in step (a) under conditions permissive for specific binding of a molecule in the sample of step (b) to an array-bound biological molecule; and,

(d) screening for specific binding of a molecule in the sample of step (b) to an array-bound biological molecule, thereby identifying a specific binding partner.

59. The method of claim 58, further comprising at least one wash step between the contacting of step (c) and the screening of step (d).

60. A method for generating a molecular profile of a nucleic acid sample, comprising the following steps:

(a) providing an article of manufacture comprising an array of biological molecules,

wherein, before attachment to the surface, the biological molecules are modified by reaction with a compound having the formula: $R_1 - X - R_2$, wherein R_1 is a cyclic ether group, R_2 is an alkoxysilane group and X is a moiety chemically suitable for linking the cyclic ether group and the alkoxysilane group, and the modified biological molecules are covalently bound to the surface;

(b) providing a sample comprising a nucleic acid; and

(c) contacting the nucleic acid with the array-bound biological molecules as set forth in step (a) under conditions, allowing binding of the sample nucleic acid to the array-bound biological molecules, and detecting binding of the sample nucleic acid to the array-bound biological molecules, thereby generating a molecular profile of the sample nucleic acid.

61. The method of claim 60, wherein the array-bound biological molecules comprise a nucleic acid.

62. The method of claim 61, wherein the binding comprises hybridization of the sample nucleic acid to the array-bound nucleic acid.

63. The method of claim 61, wherein the array-bound nucleic acid is derived from a genomic DNA.

64. The method of claim 61, wherein the array-bound nucleic acid represents a section of at least one a chromosome or at least one substantially complete chromosome.

65. The method of claim 64, wherein the chromosome is a human chromosome.

66. The method of claim 64, wherein the array-bound nucleic acids have been mapped to a known location on a chromosome.

67. The method of claim 61, wherein the molecular profile is a comparative genomic hybridization (CGH).

68. The method of claim 61, wherein the molecular profile comprises detection of a genomic DNA amplification, a genomic DNA deletion, or a genomic DNA insertion.

69. The method of claim 61, wherein the molecular profile comprises detection of a point mutation.

70. The method of claim 61, wherein the molecular profile is the identification of a single-nucleotide polymorphism (SNP).

71. The method of claim 69, wherein the detection of a point mutation comprises a primer extension assay.

72. The method of claim 61, wherein the array-bound nucleic acids are CpG island tags and the molecular profile is a differential methylation hybridization (DMH).

73. The method of claim 72, wherein the sample nucleic acids comprise genomic DNA digested with at least one methylation-sensitive restriction endonuclease and the molecular profile comprises detection and mapping of hypermethylated regions of the genome.

74. The method of claim 73, wherein the methylation-sensitive restriction endonuclease is selected from the group consisting of NotI, SmaI, SacII, EagI, MspI, HpaII and BssHII..

75. The method of claim 61, wherein the molecular profile comprises detection of transcriptionally active regions of a genome.

76. The method of claim 75, wherein the sample of nucleic acid is derived from a nuclear run-off assay.

77. The method of claim 61, wherein the molecular profile comprises an analysis of a chromatin structure.

78. The method of claim 61, wherein the array-bound biological molecule comprises a chromatin structure.

79. The method of claim 61, wherein the molecular profile comprises an analysis of a telomeric structure.

80. The method of claim 79, wherein the molecular profile of telomeric structure comprises an analysis of telomeric erosion or telomeric addition.

81. The method of claim 61, wherein the array-bound biological molecule comprises a telomere structure.

82. A method for making a modified biological molecule comprising
(a) providing a biological molecule;

(b) providing a compound having the formula: $R_1 - X - R_2$, wherein R_1 is a cyclic ether group or an amino group, R_2 is an alkoxysilane group and X is a moiety chemically suitable for linking the cyclic ether group or the amino group to the alkoxysilane group; and

5 (c) reacting the biological molecule with the compound, thereby modifying the biological molecule with the compound.

83. A method for making an article of manufacture comprising an arrayed plurality of biological molecules covalently bound to a surface comprising

(a) providing a biological molecule;

10 (b) providing a compound having the formula: $R_1 - X - R_2$, wherein R_1 is a cyclic ether group or an amino group, R_2 is an alkoxysilane group and X is a moiety chemically suitable for linking the cyclic ether group or the amino group to the alkoxysilane group;

(c) providing a surface comprising hydroxyl groups;

15 (d) reacting the biological molecule with the compound, thereby modifying the biological molecule with the compound; and

(e) depositing a plurality of modified biological molecules on the surface as discrete clusters, wherein a modified biological molecule is attached to the surface on at least one discrete and known location to form a cluster of substantially identical biological
20 molecules and the array comprises a plurality of clusters.